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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 24 2007

WARNING LETTER

VIA FEDERAL EXPRESS

Mathias AL Fobi, M.D.
Center for Surgical Treatment of Obesity
21520 S. Pioneer Boulevard, Suite 204
Hawaiian Gardens, CA 90716

Dear Dr. Fobi:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from September 19 through 29, 2006, by an investigator from the Los Angeles District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study [redacted], sponsored by [redacted] complied with applicable federal regulations. The [redacted] is a device as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also requests prompt corrective action to address the violations cited.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval applications (PMA), and Premarket Notification submissions [510(k)] are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812 – Investigational Device Exemptions, and Part 50 – Protection of Human Subjects. At the close of the inspection, the FDA investigator presented an inspectional observations Form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the Form FDA 483 and our subsequent review of the inspection report are discussed below:

Failure to obtain informed consent in accordance with the regulations regarding the protection of human subjects [21 CFR 50.20].

Pursuant to 21 CFR 50.20, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

Between [redacted] and [redacted] 175 subjects were implanted with the investigational device without being provided with an informed consent form (ICF) meeting the requirements of 21 CFR part 50; many of these subjects signed consents for surgery but these documents did not indicate that they were participating in a clinical investigation or otherwise fulfill the requirements of the FDA regulations. Between [redacted] and [redacted], eight subjects implanted with the investigational device signed an ICF for which there is no indication of IRB approval, as required by 21 CFR 50.27(a).

Failure to obtain IRB and FDA approval prior to allowing subjects to participate in an investigation [21 CFR 812.110(a)].

Pursuant to 21 CFR 812.110(a), an investigator shall not allow any subject to participate in an investigation before obtaining IRB and FDA approval. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

The FDA granted a conditional approval of [redacted] and full approval on [redacted]. The IRB at [redacted] approved the protocol on [redacted]. However, you began implanting subjects with the investigational device on [redacted], implanting 185 subjects prior to the conditional approval granted by the FDA on [redacted] and IRB approval granted on [redacted].

Failure to ensure that an investigation is conducted according to the signed agreement, investigational plan, and applicable FDA regulations [21 CFR 812.100]; 812.110(b)].

Pursuant to 21 CFR 812.100 and 812.110(b), an investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, investigational plan, and applicable FDA regulations. Examples of your failure to adhere to the above stated regulations include but are not limited to the following:

A. The investigation was initiated in [redacted] without FDA or IRB approval and before an investigator agreement was signed. One hundred eighty five subjects were implanted prior to the conditional approval granted by the FDA on [redacted] and IRB approval which was granted on [redacted].

B. Adverse events were not communicated by telephone to the sponsor and the IRB or confirmed in writing with 5 days of occurrence as required by the protocol.

i Subject[ ] implanted on[ ]under the protocol approved by the IRB, suffered a small bowel obstruction on[ ] but as of the date of the inspection, this had not been reported to the sponsor and IRB, as required by the protocol.

ii. Subject[ ] implanted on[ ]under the protocol approved by the IRB, suffered a deep vein thrombosis on[ ], but as of the date of the inspection, this had not been reported to the sponsor and IRB, as required by the protocol.

Failure to ensure that an investigational device is used only with subjects under the investigator's supervision and is not supplied to any person not authorized under this part to receive it [21 CFR 812.110(c)].

Pursuant to 21 CFR 812.110(c), an investigator shall only permit an investigational device to be used with subjects under his supervision and shall not supply an investigational device to any person not authorized under this part to receive it. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

Subjects[ ], and[ ]were implanted with the investigational device by physicians other than you, the principle investigator, and there is no documentation that these physicians or the subjects were under your supervision.

Failure to maintain complete records of receipt, use, and disposition of an investigational device [812.140(a)(2)].

Pursuant to 21 CFR 812.140(a)(2), an investigator is responsible for maintaining records of receipt, use or disposition of a device that relate to the type and quantity of the device, the dates of its receipt and the batch number or code mark, the names of all persons who received, used, or disposed of each device, and why and how may units of the device have been returned to the sponsor, repaired, or otherwise disposed of. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

There were no records of device accountability available for review during the inspection due to the fact that no records were maintained of the number of investigational devices received by Dr. Fobi, number of devices implanted, the number of devices discarded, or the number of devices currently on hand.

Failure to submit progress reports at the required intervals to the reviewing IRB [21 CFR 812.150(a)(3)].

Pursuant to 21 CFR 812.150(a)(3), an investigator shall prepare and submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular

intervals, but in no event less often than yearly. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

[redacted] IRB approval letter dated [redacted], required quarterly reports be submitted, with the first due on July 12, 2006. As of the close of the inspection on 9/28/06, no reports had been submitted to the IRB.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to: Attention: Doreen Kezer, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to the Los Angeles district office, 19701 Fairchild, Irvine, CA 92612. Please send a copy of your response to that office.

If you have any questions, please contact Doreen Kezer, (240) 276-0125, doreen.kezer@fda.hhs.gov.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and Radiological Health

cc: [redacted] (purged copy)
[redacted]

[redacted] (purged copy)
[redacted]